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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,870	04/12/2001	Masad J. Damha	1770-206US FC	5859

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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 06/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,870	DAMHA ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5-17,19,20 and 35-42* is/are pending in the application.

4a) Of the above claim(s) *7-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5,6,19,20 and 35-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 December 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3-03-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 2-3, 5-6, 7-17 (withdrawn), 19-20, and 35-42 (new) are currently pending.

Continued Examination Under 37 CFR 1.114

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3-03-05 has been entered.

Drawings

4. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because Figure 4 is unclear, the information in the Figure cannot be understood. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Response to Arguments

Claim Rejections - 35 USC § 102/103

5. Claims 2, 5-6, and 19 remain rejected under 35 U.S.C. 102(b)/103(a) as being anticipated by or obvious over McCormick (US Patent No. 4,760,017).

The instant claims are drawn to a composition to selectively prevent or modulate gene expression in a sequence specific manner; which comprises an effective amount of at least one oligonucleotide selected from the group consisting of an oligonucleotide consisting of β-D-arabinose sugars hybridizing to a complementary RNA to induce RNAse H activity, an oligonucleotide consisting of β-arabinose sugars substituted at 2' position of the sugar ring with halogen, alkyl, CH_2F, CF_3, SCH_3, allyl, amino, aryl, alkoxy, or azido and hybridizing to duplex DNA/DNA or DNA/RNA to induce RNase H activity, and an oligonucleotide consisting of β-D-arabinose sugars substituted at 2' position of the sugar ring with halogen, alkyl, CH_2F, CF_3, SCH_3, allyl, amino, aryl, alkoxy, or azido and hybridizing to duplex DNA/DNA or DNA/RNA to form a triple helical complex, in associated with an acceptable carrier.

6. Applicant's arguments filed 3-03-05 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that "there is no teaching of compositions of arabinonucleosides or derivatives thereof, including the presently claimed oligonucleotides consisting of β-D-arabinose sugars substituted at 2' position of the sugar ring, for the purpose of binding RNA to elicit RNase H activity in the reference of McCormick. Rather, McCormick teaches arabinonucleosides (ANA) can be used as probes for single-stranded DNA or RNA..."

In response to applicant's argument that the arabinonucleosides of McCormick are not disclosed "for the purpose of binding RNA to elicit RNase H activity," a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). As stated previously, β-D-arabinonucleosides are used in the synthesis of the arabinonucleic acid probes of McCormick, see Example 1. Although, the McCormick reference does not specifically teach that the arabinonucleic probes can be used to induce RNAse H activity, the probes of this reference meet all the structural limitations of Applicant's invention, particularly wherein it is drawn to an oligonucleotide consisting of β-arabinose sugars hybridizing to a complementary RNA. Additionally, the hybridization solution containing the arabinonucleic acid probes described in col. 8, lines 1-18, can be considered an acceptable carrier of the oligonucleotides consisting of β-arabinose sugars as recited in the instant claims.

Applicants further traverse the instant rejection on the following grounds: (1) the McCormick reference does not necessarily teach in every instance the formation of duplexes with arabinonucleosides probes that could induce RNase H activity, i.e., the preparation of DNA/RNA heteroduplexes; (2) there is nothing in McCormick that directly evidences the presence of RNAse H in the compositions of McCormick; (3) neither McCormick nor any other prior art has taught or suggested the use of antisense ANA's for cleaving hybridized RNA by RNase H as claimed in the present invention.

Contrary to Applicant's assertions, the claimed invention is essentially drawn to a composition comprising oligonucleotides consisting of β-D-arabinonucleosides, oligonucleotides comprising β-D-arabinose sugars substituted at the 2' position, in association with an acceptable carrier, the limitations associated with the intended use of the claimed β-D-arabinonucleoside

oligonucleotides, namely wherein the oligonucleotides induce RNase H or form a triple helical complex, are not considered to patentably distinguish the claimed invention from the prior art. The prior art clearly teaches that the disclosed arabinonucleosides are capable of forming structures with complementary DNA or RNA, see col. 7, lines 5-26 of McCormick. Moreover, the instant claims do not require the presence of RNase H in the claimed compositions. Therefore, absent evidence to the contrary, the oligonucleotides of McCormick are considered to meet the limitations of the claimed inventions to the extent that the claims read on a composition comprising β-D-arabinonucleoside oligonucleotides in an acceptable carrier.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 2, 5-6, 19, 35, 38, 40 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilds et al.

Wilds et al. disclose 2'F-arabino-β-D-arabinofuranosyl oligonucleotides in solution (see page 300 (General Methods and Figure 1). These oligonucleotides are disclosed as functioning to elicit RNase H activity when bound to single stranded RNA, and to for triplex structures (see Summary on page 303).

Claim Rejections - 35 USC § 103

9. Claims 2-3, 5-6, 19, and 35, 38, and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheng et al. (US Patent No. 5,646,126) in view of Wilds et al.

Cheng et al. describe oligonucleotides comprising 2'-deoxy, 2'-fluoro or 2'-difluoro nucleosides, wherein between 8 and 18 of said nucleosides are linked consecutively, see Figure 1, formula 2, see also claim 1. Specifically, the compounds of Cheng et al. encompasses wherein the R1 and R2 substituents of the 2' position of the nucleosides comprises either H or F, or wherein both R1 and R2 are F (fluorine) see col. 63, lines 24-25. Additionally, Cheng et al. teach that ODNs (oligonucleotides) including α and β arabinosides, are included within the scope of the invention (col. 9, lines 33-39).

Cheng et al. does not specifically disclose isolated oligonucleotides comprising arabinose sugars and 2'-fluoro or 2'-difluoro modified nucleosides consecutively linked in the same molecule.

Wilds et al. disclose 2'F-arabino-β-D-arabinofuranosyl oligonucleotides in solution (see page 300 (General Methods and Figure 1). These oligonucleotides are disclosed as functioning to elicit RNase H activity when bound to single stranded RNA, and to for triplex structures (see Summary on page 303). Wilds et al. also teach that these oligonucleotides have increased nuclease resistance in comparison to DNA, and enhanced stability in comparison to DNA and RNA, see page 303.

It would have been obvious to one of ordinary skill in the art at the time of filing to modify the oligonucleotides of Cheng et al. with the teachings of Chu et al. to produce the compositions of the present invention. It would have been obvious to modify the

oligonucleotides of Cheng et al. to comprise 2'-difluoro or 2'-fluoro arabinosyl nucleosides because, Cheng et al. expressly teach that their disclosed invention encompasses oligonucleotides comprising or including α and β arabinosides. Moreover, one of ordinary skill in the art seeking to enhance the properties of an oligonucleotide would have been motivated to modify the teachings of Cheng et al. to design the compounds of the present invention because Wilds et al. teach that oligonucleotide stability can be increased by introducing 2'-deoxy-2'-β-D-fluoro-arabinofuranosyl nucleosides into the oligonucleotide structure. One of ordinary skill in the art would have had a reasonable expectation of success in designing the compounds according to the present invention, since WIlds et al. describes the synthetic steps necessary for introducing 2'-deoxy-2'-fluoro-arabinofuranosyl moieties into an oligonucleotide structure.

Therefore, the invention as a whole would have been *prima facie* obvious over Cheng et al. in view of Wilds et al.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 20, and 36-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36-37 recite "an oligonucleotide consisting of β-D arabinose sugars" there is no antecedent basis for wherein the oligonucleotide has "at least one 2-O-methyl-D-ribose sugar."

Claim 20 recites an oligonucleotide "consisting of" a particular formula, there is no antecedent basis for wherein the formula has at least one 2-O-methyl-D-ribose sugar, since the formula recites 2'-difluoro arabinose sugars.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Patent Examiner
Art Unit 1635

JLE